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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/287,500	04/07/99	LEE J	STK-1-DIV-3

EXAMINER	
ROMEO, D	
ART UNIT	PAPER NUMBER
1647	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/287,500	Lee et al.
Examiner	**Art Unit**
David Romeo	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *20 Jul 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *69-88, 90, 91, and 93-105* is/are pending in the application.

4a) Of the above, claim(s) *72, 73, 81, 82, 88, and 93-101* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *69-71, 74-80, 83-87, 90, 91, and 102-105* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *69-88, 90, 91, and 93-105* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *10*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. The amendment filed 07/20/2001 (Paper No. 9) has been entered. Claims 69-88, 90, 91, 93-105 are pending. Claims 69-88, 90, 91, 93-101 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species and/or invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6. Claims 69-71, 74-80, 83-87, 90, 91, 102-105 are being examined to the extent that they read upon the elected species and/or invention.

2. Claims 69-71, 74-80, 83-87, 90, 91, 102-105 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing bone formation, does not reasonably provide enablement for a method of inducing tissue formation, repair, or integration without regard to the tissue whose formation, repair, or integration is induced or for a method of treating a tissue degenerative condition without regard to the tissue treated. Applicants' arguments have been fully considered but they are not persuasive. The claims are not limited to the regeneration of bone, tendon, or ligaments but encompass the regeneration of any and all tissues. The cells in an embryo are unlike the cells in an adult because the cells in an embryo are undifferentiated and many cytokines that subserve familiar functions postnatally play different or unknown roles embryologically and given the amino acid sequence of a cytokine and any of its actions one cannot predict when or where it will do what else. Example

13 provides an assay in which the artisan could test nerve regeneration. Example 13 does not demonstrate nerve regeneration, and nerve cells are retained throughout adult life and seem never to divide and cannot be replaced if lost.

3. Claims 77-80, 83-87, 90, 91, 105 are indefinite because they lack a process step which clearly relates back to the claim preamble and it is unclear what process is to be achieved; an intended use is not the same as achieving a result; in the absence of a recitation as to any result, or a process step producing a result, it is unclear what result of the process can be inferred. Applicants' arguments have been fully considered but they are not persuasive. It is unclear what treatment is inferred by the term "treats".

4. Claims 69-71, 77-80, 83-87 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang (b7)[1]. Applicants argue that Wang does not teach the use of IGF-I at a concentration effective to stimulate BMP-2 activity. All that the claims require is a morphogen and IGF-I, which is what Wang teaches. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies

[1]Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

(i.e., stimulate BMP-2 or OP-1 activity, stimulation of AP activity) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. Applicants arguments regarding IGF-II do not appear to be germane to the rejection. In addition, TGF-β and BMP synergize in promoting formation of endochondral bone in vivo. See Ogawa (u11), page 14233, paragraph bridging columns 1-2.

5. Claims 77, 85 are rejected under 35 U.S.C. 102(e) as being anticipated by Kuberasampath (e7). Applicants argue that "stimulate" means "synergism" and Kuberasampath does not teach "synergism". Applicants' arguments have been fully considered but they are not persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., synergism) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. There is nothing in the instant specification to distinguish the term "beneficial" from the term "MPSF". In addition, TGF-β and BMP synergize in promoting formation of endochondral bone in vivo, suggesting that TGF-β is an MPSF. See Ogawa (u11), page 14233, paragraph bridging columns 1-2.

6. Claims 74, 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (b7) in view of Kuberasampath (c7). Applicants' arguments have been fully considered but they are

not persuasive. No difference is seen between "agents beneficial to the treatment of the bone defects", i.e. IGF-I, and a "MPSF".

7. Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rueger (d7) in view of Wang (b7). Applicants' arguments have been fully considered but they are not persuasive. No difference is seen between "agents beneficial to the treatment of the bone defects", i.e. IGF-I, and a "MPSF".

8. Claims 77, 90, 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (e7) as applied to claim 77 above and further in view of Hock (w7) and further in view of Baylink (a7) or Wang (b7). Applicants' arguments have been fully considered but they are not persuasive. No difference is seen between administering OP-1 together with other "co-factors" known to have a beneficial effect on bone remodeling such as IGF-I, and administering OP-1 together with an "MPSF". One of ordinary skill in the art would have a reasonable expectation that a composition comprising OP-1 and IGF-I would not only have an additive effect on the proliferation and differentiation of bone cells, but would create a surprisingly marked synergism as well.

New formal matters, objections, and/or rejections:

Claim Rejections - 35 USC § 103

9. Claims 69, 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (b7) as applied to claim 69 above and further in view of Kuberasampath (n11). Wang (b7) teaches a method of administering a composition comprising a carrier, a morphogen and IGF-I, as discussed above. Wang (b7) does not teach a carrier comprising heparin. Kuberasampath (n11) teaches a device comprising a carrier comprising heparin (page 5, full paragraph 1; paragraph bridging pages 5-6). Kuberasampath (n11) does not teach a method of administering a composition comprising a carrier, a morphogen and IGF-I. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer a composition comprising a carrier, a morphogen and IGF-I, as taught by Wang (b7), and to modify that teaching by administering a composition comprising a carrier comprising heparin, as taught by Kuberasampath (n11), with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to induce the formation of endochondral bone in a mammalian host in a shape conforming substantially to the shape of the device or in order to use the device as a surface coating for implantable prosthetic devices to promote cellular ingrowth. The invention is prima facie obvious over the prior art.

10. Claims 77, 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (e7) as applied to claim 77 above and further in view of Kuberasampath (n11).

Kuberasampath (e7) teaches a method of administering a composition comprising a carrier, a morphogen and IGF-I, as discussed above. Kuberasampath (e7) does not teach a carrier comprising heparin. Kuberasampath (n11) teaches a device comprising a carrier comprising heparin (page 5, full paragraph 1; paragraph bridging pages 5-6). Kuberasampath (n11) does not teach a method of administering a composition comprising a carrier, a morphogen and IGF-I. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer a composition comprising a carrier, a morphogen and IGF-I, as taught by Kuberasampath (e7), and to modify that teaching by administering a composition comprising a carrier comprising heparin, as taught by Kuberasampath (n11), with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to induce the formation of endochondral bone in a mammalian host in a shape conforming substantially to the shape of the device or in order to use the device as a surface coating for implantable prosthetic devices to promote cellular ingrowth. The invention is prima facie obvious over the prior art.

11. Claims 74, 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (b7) in view of Kuberasampath (c7) as applied to claim 74 above and further in view of Kuberasampath (n11). Wang (b7) in view of Kuberasampath (c7) teaches a method of administering a composition comprising a carrier, a morphogen and IGF-I, as discussed above.

Wang (b7) in view of Kuberasampath (c7) does not teach a carrier comprising heparin. Kuberasampath (n11) teaches a device comprising a carrier comprising heparin (page 5, full paragraph 1; paragraph bridging pages 5-6). Kuberasampath (n11) does not teach a method of administering a composition comprising a carrier, a morphogen and IGF-I. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer a composition comprising a carrier, a morphogen and IGF-I, as taught by Wang (b7) in view of Kuberasampath (c7), and to modify that teaching by administering a composition comprising a carrier comprising heparin, as taught by Kuberasampath (n11), with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to induce the formation of endochondral bone in a mammalian host in a shape conforming substantially to the shape of the device or in order to use the device as a surface coating for implantable prosthetic devices to promote cellular ingrowth. The invention is prima facie obvious over the prior art.

12. Claims 76, 104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rueger (d7) in view of Wang (b7) as applied to claim 76 above and further in view of Kuberasampath (n11). Rueger (d7) in view of Wang (b7) teaches a method of administering a composition comprising a carrier, a morphogen and IGF-I, as discussed above. Rueger (d7) in view of Wang (b7) does not teach a carrier comprising heparin. Kuberasampath (n11) teaches a device

comprising a carrier comprising heparin (page 5, full paragraph 1; paragraph bridging pages 5-6). Kuberasampath (n11) does not teach a method of administering a composition comprising a carrier, a morphogen and IGF-I. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer a composition comprising a carrier, a morphogen and IGF-I, as taught by Rueger (d7) in view of Wang (b7), and to modify that teaching by administering a composition comprising a carrier comprising heparin, as taught by Kuberasampath (n11), with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to induce the formation of endochondral bone in a mammalian host in a shape conforming substantially to the shape of the device or in order to use the device as a surface coating for implantable prosthetic devices to promote cellular ingrowth. The invention is prima facie obvious over the prior art.

13. Claims 77, 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (e7) as applied to claim 77 above and further in view of Hock (w7) and further in view of Baylink (a7) or Wang (b7) and further in view of Kuberasampath (n11). Kuberasampath (e7) as applied to claim 77 above and further in view of Hock (w7) and further in view of Baylink (a7) or Wang (b7) teaches a method of administering a composition comprising a carrier, a morphogen and IGF-I, as discussed above. Kuberasampath (e7) as applied to claim 77 above and further in view of Hock (w7) and further in view of Baylink (a7) or Wang (b7) does not teach a

carrier comprising heparin. Kuberasampath (n11) teaches a device comprising a carrier comprising heparin (page 5, full paragraph 1; paragraph bridging pages 5-6). Kuberasampath (n11) does not teach a method of administering a composition comprising a carrier, a morphogen and IGF-I. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer a composition comprising a carrier, a morphogen and IGF-I, as taught by Kuberasampath (e7) as applied to claim 77 above and further in view of Hock (w7) and further in view of Baylink (a7) or Wang (b7), and to modify that teaching by administering a composition comprising a carrier comprising heparin, as taught by Kuberasampath (n11), with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to induce the formation of endochondral bone in a mammalian host in a shape conforming substantially to the shape of the device or in order to use the device as a surface coating for implantable prosthetic devices to promote cellular ingrowth. The invention is prima facie obvious over the prior art.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. This application contains claims drawn to a nonelected invention or inventions. A complete reply to the final rejection must include cancellation of nonelected claims and/or inventions or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

OCTOBER 8, 2001